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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,879	05/22/2001	Kazuya Katagai	MUR-026-USA-	8324

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DONALD E. TOWNSEND
601 Pennsylvania Avenue, N.W.
Suite 900, South Building
Washington, DC 20004

EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,879	KATAGAI ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-12,14 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5-12, 14, and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendments to the Specification and Claims received on March 30, 2004 is acknowledged. Claims **1, 3, 5-12, 14, and 17** are pending in this application. Claim 13 is withdrawn. Claims 2, 4, and 15-16 are cancelled.

Specification

The amendment filed March 30, 2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Applicant has added ethylene glycol diglycidylether to example 6 and has amended the weight percent accordingly, however applicant does not have support for this amendment. The examiner notes that the foreign priority papers page 30 do not support this amendment.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

Claims 1, 3, 5-12, 14, and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites the drug to acidic polymer as 2:1 to 1:3; however applicant does not have support for this range. After a careful review of the instant specification the examiner finds support for 10:1 to 1:10, 5:1 to 1:5, and 3:1 to 1:3 on page 10 respectively. However, the instant

range is considered new matter. If applicant contends this range is not new matter, then the specific line and page for said support is requested.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 depends on canceled claim 2 and thus the limitation of this claim is vague and indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/24352.

WO discloses a patch containing pridinol (basic drug) or its salt in the amount of 0.01-5% in a patch formulation. See abstract and page 1 of translation. The patch contains water-soluble polymer in the amount of 5-20%. The water-soluble polymers disclosed are gelatin, carboxyl vinyl polymer, and methyl vinyl ether maleic anhydride copolymer. See page 4 and examples, especially 7 and 10. The humectant disclosed is glycerin and polyethylene glycol (PEG) in the amount of 30-60%. See page 5 and examples. Water is utilized in the amount of 25 to 55%

preferably. See page 6 and examples. Lastly, a multifunctional epoxy compound cross-linking agent in the amount of 0.02-3% preferably is disclosed on page 7 and examples.

Note that the preamble "adhesive gel composition for an iontophoresis" is not given patentable weight since it is provides an intended use without a structural limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 5-12 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/24352 in view of Linkwitz et al (6,295,469).

WO discloses a patch containing pridinol or its salt in the amount of 0.01-5% in a patch formulation for transdermal administration. See abstract and page 1 of translation. The patch contains water-soluble polymer in the amount of 5-20%. The water-soluble polymers disclosed are gelatin, carboxyl vinyl polymer, and methyl vinyl ether maleic anhydride copolymer. See page 4 and examples, especially 7 and 10. The humectant disclosed is glycerin and polyethylene

glycol (PEG) in the amount of 30-60%. See page 5 and examples. Water is utilized in the amount of 25 to 55% preferably. See page 6 and examples. A multifunctional epoxy compound cross-linking agent in the amount of 0.02-3% preferably is disclosed on page 7 and examples. WO teaches the use of anti-oxidants in the formulation. See page 9.

WO does not teach the use of instant drugs or instant antioxidants.

Linkwitz et al teach a formulation for electrically assisted delivery of lidocaine and epinephrine. Linkwitz teaches the presence of epinephrine helps retard adsorption of lidocaine, thereby reducing its systemic toxicity. Epinephrine also increases the duration of the drug's local anesthetic effect. The vasoconstrictive effect of epinephrine maintains localization of lidocaine a the nerve, thereby prolonging the effect of action of lidocaine. See column 1, lines 40-55. Lidocaine is utilized in the amount of 1-10% and about 0.01-0.2% epinephrine. See column 3, lines 20-28. Further, Linkwitz teaches that epinephrine is degraded by oxygen and reduces the storage ability of lidocaine. To enhance the stability, the reference teaches the use of antioxidants such as sodium metabisulfite in the amount of 0.01-0.2%. see column 4, lines 20-35.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of WO and Linkwitz et al and utilize the instant active agents in WO's formulation. One would be motivated to do so since Linkwitz teaches that epinephrine provides prolonged effect of an analgesic such as instant lidocaine, for transdermal administration. Firstly, it is prima facie obvious to substitute a known trandermally administrable active agent, such as instant lidocaine and/or epinephrine, in WO's formulation since it is also utilized for the same purpose: for the transdermal administration of drugs. Secondly, it is prima facie obvious to combine the instant lidocaine with instant epinephrine to prolong the effect of

the analgesic, i.e. lidocaine. Lastly, Linkwitz establishes the state of the art wherein it is known in the art to utilize the instant combination for administering drugs across the skin, i.e. transdermally.

In regards to the instant antioxidant, sodium hydrogen sulfite and Linkwitz's antioxidant sodium metabisulfite are obvious substitutions of each other.

Claims 11 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/24352 in view of Linkwitz et al (6,295,469) in further view of JP 08-325149.

As set forth above, WO discloses a patch containing pridinol or its salt in the amount of 0.01-5% in a patch formulation for transdermal administration. See abstract and page 1 of translation. WO teaches the use of anti-oxidants in the formulation such as ascorbic acid, BHT, tocopherol, etc.. See page 9.

As set forth above, Linkwitz et al teach a formulation for electrically assisted delivery of lidocaine and epinephrine. Linkwitz teaches the presence of epinephrine helps retard adsorption of lidocaine, thereby reducing its systemic toxicity. Epinephrine also increases the duration of the drug's local anesthetic effect. The vasoconstrictive effect of epinephrine maintains localization of lidocaine a the nerve, thereby prolonging the effect of action of lidocaine. See column 1, lines 40-55. Lidocaine is utilized in the amount of 1-10% and about 0.01-0.2% epinephrine. See column 3, lines 20-28. Further, Linkwitz teaches that epinephrine is degraded by oxygen and reduces the storage ability of lidocaine. To enhance the stability, the reference teaches the use of antioxidants such as sodium metabisulfite in the amount of 0.01-0.2%. see column 4, lines 20-35.

The reference do not specify the instant antioxidant.

JP teaches an external preparation containing an active agent (pridinol), water-soluble polymers (polyacrylic acid polymer), polyhydric alcohols (glycerol/ benzyl alcohol blend), and antioxidant (sodium hydrogen sulfite). Crosslinking agents such as organic acid or salt of an organic acid are included in the composition. See Detailed Description in its entirety). The instant ratio of drug to polymer is taught in the examples. JP teaches a stabilizing agent such as instant sodium hydrogen sulfite, L-ascorbic acid, tocopherol, instant sodium hydrogen sulfite, BHT, etc. see page 8.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the teachings of JP 08-325149 and incorporate its teaching into WO and utilize the instant antioxidant. One would be motivated to do so since JP teaches the functional equivalency of the instant antioxidant and WO's antioxidants. Therefore, it is prima facie obvious to substitute an equivalent antioxidant for the prior art's antioxidant with the expectation of similar results since the prior art establishes functional equivalency.

The rejection of claims 1, 3, 5, and 14 under 35 U.S.C. 103(a) as being unpatentable over Oda et al (5,725,874) is maintained.

Oda et al teach an external preparation that contains a)0.001-20% of a drug, b) 1-30% of a water-soluble polymer in the amount of 1-30% such as polyacrylic acid, isobutylenemaleic anhydride copolymer, or gelatin, d) water, and e) polyhydric alcohol. See column 3. The base may include a crosslinking agent such as a polyfunctional epoxy compound. See column 4, lines 13-30. The preferable amount of drug is 0.001-20 and more preferably 0.5-10% and the water-soluble polymer in the amount of 1-30%, preference to 1-20%, and ideally 1-15%. Further,

antioxidants such as ascorbic acid, tocopherol, etc. are taught. See column 4, lines 35-40. Among the drugs taught is instant lidocaine. See column 3, line 11.

The reference does not exemplify a composition containing the crosslinking agent.

It is deemed obvious to one of ordinary skill in the art at the time the invention was made to include the crosslinking agent in the composition. One would be motivated to do so with the expectation of similar results since Oda clearly suggests the incorporation of crosslinking agents.

Response to Arguments

Applicant argues that Oda et al fails to disclose the instant ratio as amended. Further, applicant argues that Oda's drug is dissolved in an oily phase such as that an electromotive force cannot affect the drug. Thus, this is in contrast to the present invention and Oda's composition cannot be used as a donor gel. Lastly, applicant argues unexpected results in the specification.

Applicant's argument have been fully considered but they are not persuasive. Firstly, the examiner points out that Oda's range of the drug to water-soluble polymer falls within the instant range. Applicant's preferred range of the polymer is 1-20% and preferably 1-10% and the prior art teaches a range of 1-20 with a preference for 1-15%. Applicant's preferred range in the specification for lidocaine is 1-20 and preferably 1-10% whereas prior art's is 0.001-20% and 0.5-10%. Clearly this falls within instant range. Further, the examples utilize the instant range. T

Secondly, it is pointed out that the argument that "Oda's drug is dissolved in an oily phase such as that an electromotive force cannot affect the drug" is moot since applicant is relying on a feature that is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore,

the recitation "for an iontophoresis" in the preamble is not given weight since it is an intended use limitation.

Lastly in regards to the unexpected results, the examiner points out that firstly the unexpected results are not a direct comparison with the prior art to show a superior result. Secondly, it should be noted that if one were to say that there is an unexpected effect, the instant claims are not commensurate in scope. For instance, applicant independent claims recite a generic drug whereas the examples in the specification utilize specifically lidocaine and epinephrine. Further, applicant utilizes specific weight percents to provide the effect. Thus, the claims are not commensurate in scope.

Claims 5-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oda et al (5,725,874) in view of Lugnani et al (5,843,016).

Oda et al teach an external preparation that contains a)0.001-20% of a drug, b) 1-30% of a water-soluble polymer in the amount of 1-30% such as polyacrylic acid, isobutylenemaleic anhydride copolymer, or gelatin, d) water, and e) polyhydric alcohol. See column 3. The base may include a crosslinking agent such as a polyfunctional epoxy compound. See column 4, lines 13-30. The preferable amount of drug is 0.001-20 and more preferably 0.5-10% and the water-soluble polymer in the amount of 1-30%, preference to 1-20%, and ideally 1-15%. Further, antioxidants such as ascorbic acid, tocopherol, etc. are taught. See column 4, lines 35-40. Among the drugs taught is instant lidocaine. See column 3, line 11.

Lugnani et al teach a method of treating acute urinary obstruction utilizing electromotive (transdermal) drug administration. See abstract. The reference teaches the use of various drugs for transdermals such as analgesic drugs, i.e. lidocaine, mepivacaine, bupivacine, and

ropivacaine in the amount of 0.3-1%. Furthermore, Lugnani teaches the use of the analgesics with epinephrine in a concentration of 1/200000-1/50000 in order to achieve a prolonged effect. See column 11, lines 49-56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Oda et al and Lugnani et al and utilize the instant active agents in Oda's formulation. One would be motivated to do so since Lugnani teaches that epinephrine provides prolonged effect of an analgesic such as instant lidocaine. Therefore, it is prima facie obvious to combine the instant lidocaine with epinephrine to prolong the effect of the analgesic. Further, one would expect similar results since both references provide for transdermal administration of the active agents and Lugnani establishes the state of the art wherein it is known in the art to utilize the instant combination.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

MICHAEL G. HARTLEY
PRIMARY EXAMINER